

REMARKS

Claims 1-30 and 33-34 are pending. In the Office Action dated January 26, 2004, the Examiner rejected claims 1-30 and 33-34. Applicants thank the Examiner for the courtesy of the telephonic interview of April 20, 2004, the contents of which are incorporated in the remarks below.

In light of the following remarks, Applicants respectfully request reconsideration and allowance of claims 1-30 and 33-34.

Rejections under 35 U.S.C. § 103

The Examiner rejected claims 1-19 and 21-30 under 35 U.S.C. §103(a) as being unpatentable over Gaynor *et al.* (U.S. 5,904,924) ("Gaynor"), and rejected claims 1-34 under 35 U.S.C. §103(a) as being unpatentable over Perkes (WO 99/07400) ("Perkes"). In particular, the Examiner acknowledged that neither Gaynor nor Perkes expressly teaches the inclusion of a Muscat variety grape seed extract in nutritional supplements or the claimed ratios of grape skin extract to grape seed extract. The Examiner went on to state, however, that it was not inventive to discover the inclusion of a particular grape seed variety or an optimum range, both of which the Examiner asserted could be discovered by routine experimentation, absent a showing of criticality.

Applicants respectfully disagree. Proper analysis under § 103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition, and (2) whether the prior art would also have revealed that in so making, those of ordinary skill would have had a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Claim 1 recites a dietary supplement comprising a grape skin extract and a Muscat variety grape seed extract. Claims 25 recites a dietary supplement containing a grape skin extract and a grape seed extract where the ratio of grape skin extract to grape seed extract is between 3 to 1 and 5 to 1. The only composition disclosed in the Gaynor reference is a 969 gram mixture containing 300 mg of grape skin extract and 40 mg of grape seed extract, representing a 7.5 to 1 ratio of grape skin extract to grape seed extract. The Examiner has acknowledged that

Gaynor does not teach the claimed range of ratios of grape skin extract to grape seed extract. Applicants submit that the Examiner also has not established a *prima facie* case of obviousness based on the cited ratio, as a ratio of 7.5 to 1 is 50% larger than a ratio of 5 to 1, which represents the upper end of the claimed ratio range. Further, the Gaynor reference fails to teach or suggest any other ratio of grape skin extract to grape seed extract, or that a person having ordinary skill in the art should modify the amounts of grape skin extract and grape seed extract to obtain a supplement as presently claimed. Moreover, at no point does the Gaynor reference suggest the combination of a grape skin extract and a Muscat variety grape seed extract. In fact, the Gaynor reference never mentions combining a Muscat variety grape seed extract with a grape skin extract to form the presently claimed composition.

The Perkes reference is similarly deficient. The Perkes reference discloses three formulations containing grape skin extracts and grape seed extracts. The Perkes reference, however, does not teach or suggest any composition containing a grape skin extract in combination with a Muscat variety grape seed extract, as present claims 1-24 require. Further, at no point does the Perkes reference teach or suggest making a supplement having the claimed range of ratios of grape skin extract to grape seed extract. In fact, a person having ordinary skill in the art reading the Perkes reference would not have been motivated to make a supplement having a grape skin extract to grape seed extract ratio between 3 to 1 and 5 to 1, given that the three specific formulations exemplified in the Perkes reference have ratios (1.66 to 1, see page 17; 1.2 to 1, see page 19; and 20.5 to 1, see page 21) well outside the range of ratios presently recited in the claims. Thus, both the Gaynor and Perkes references fail to suggest that a person having ordinary skill in the art should make the presently claimed compositions.

As additional evidence of nonobviousness, Applicants note that compositions containing a Muscat grape seed extract exhibit surprisingly high reductions in platelet aggregation activity as compared to compositions containing other varieties of grape seed extracts. For example, Table 3 of the present specification (page 15) demonstrates the *in vitro* platelet inhibition activity of various grape seed extract samples, including mixtures of grape seed extracts. As can be seen, the Muscat grape seed samples (103, 136, and 156) exhibited about a two-fold or greater platelet inhibition activity as compared to six other grape seed extract samples (two individual grape seed extracts and four mixtures of grape seed extracts). In fact, Muscat grape seed extract samples

exhibited about a 3- to 12-fold greater platelet inhibition activity as compared to two Champagne grape seed extract samples (samples 165 A and 165B). Thus, Muscat grape seed extracts exhibited significantly better platelet inhibition than grape seed extracts of other varieties.

Not only do Muscat grape seed extracts exhibit substantially better platelet inhibition activity *in vitro* than other varieties, the positive platelet inhibition effects of Muscat grape seed extracts extend to *in vivo* dog studies. The Perkes reference teaches achieving reductions in platelet aggregation activity of $40\% \pm 9\%$ and $42\% \pm 10\%$ using the compositions set forth in Perkes. See Perkes reference at pages 24 and 27. Applicants' present specification, on the other hand, teaches a reduction in platelet aggregation activity of 60% with a composition having a grape skin extract in combination with a Muscat grape seed extract. See Specification at pages 18-19. As explained in the previously submitted (dated September 3, 2003) Declaration of Lynn Perkes, the difference between the $40\% \pm 9\%$ and $42\% \pm 10\%$ reductions reported in the Perkes reference and the 60% reductions reported in the present application is "substantial and unexpected."

Applicants note that although the Examiner did not expressly comment on the previously submitted Declaration of Lynn Perkes in the Office Action, the Examiner indicated that the Declaration was not persuasive in the interview of April 20, 2004. Applicants respectfully disagree. Applicants refer the Examiner to the holding in In re Soni, in which the Federal Circuit stated: "when an applicant demonstrates *substantially* improved results, as Soni did here, and *states* that the results were unexpected, this should suffice to establish unexpected results *in the absence of* evidence to the contrary." In re Soni, 54 F.3d 746, 751 (Fed. Cir. 1995) (emphasis in the original) (copy attached for the Examiner's convenience). Applicants submit that the *in vitro* and *in vivo* data discussed above demonstrate the substantially improved properties of the claimed compositions containing Muscat grape seed extracts. Further, the Declaration of Lynn Perkes states that the *in vivo* results were both "substantial and unexpected" in view of the cited Perkes compositions. As the Examiner has not set forth any evidence to rebut these unexpected results, Applicants respectfully assert that the claims are not obvious in view of either Gaynor or Perkes.

In light of the above, Applicants respectfully request the withdrawal of the rejections of claims 1-30 and 33-34 under 35 U.S.C. § 103(a).

Applicant : Suk Cho et al.
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CONCLUSION

Applicants respectfully assert that all claims are in condition for allowance, which action is requested. The Examiner is invited to telephone the under-signed if such would expedite prosecution.

Enclosed is a \$110.00 check for the Petition for Extension of Time fee (one month).
Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 5/26/04

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